UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

DATE: 12 APRIL 2006

SUBJECT: **MYCLOBUTANIL** - Occupational Human Exposure/Risk Assessment for the Use of Myclobutanil on Hops

PC Code: 128857 DP Code: 328188

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INTRODUCTION

Under provisions in § 3 of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA), as amended, the InterRegional Research Project Number 4 (IR4) and the Rohm and Haas Company have requested registration of the fungicide myclobutanil for use on hops to control downy mildew. This memorandum serves as the HED's assessment of exposure and risk to occupational pesticide handlers (mixers, loaders, applicators) and to agricultural workers.

USE PATTERN SUMMARY

The use pattern is taken from the IR4 petition ("IR-4/Myclobutanil Page 12"). The end-use-product proposed for use is Rally 40 W Agricultural Fungicide (EPA Reg. No. 707 - 221). Rally is a 40.0 % by weight, active ingredient (ai), wettable powder packaged in water soluble packages. IR4 indicates that Rally will be applied at 5.0 - 10.0 oz product per acre (0.125 - 0.25

lb ai/A). It is to be applied as a foliar spray. The lower rate is to be used when plants are small and the higher rate when plants increase in size. The application interval is 7 - 10 days. The preharvest interval (PHI) is 14 days. There is a maximum of 80 oz (5.0 lb) of Rally (2.0 lb ai) per acre per season. See Table 1.0 for a summary of the proposed use pattern.

Table 1.0 Summary of Proposed Use of Myclobutanil on Hops

Crop Site	Hops
Pest	powdery mildew
Formulation	Rally Agricultural fungicide; EPA Reg. No 707 - 221; 40.0 % wettable powder in water soluble packages
Application Method	airblast
Application Rate	0.125 - 0.25 lb ai/A
Application Number	calculated 8 possible applications at the high rate of application; 2.0 lb ai/A/season ÷ 0.25 lb ai/A/application = 8 application/season
Application Maximum	2.0 lb ai/A/season
Application Interval	7 - 10 days
Pre-Harvest Interval	14 days
Manufacturer	Rohm and Haas Company

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

Based upon the proposed use patterns, HED believes that the most highly exposed occupational pesticide handler exposures are for a mixer/loader, loading wettable powder with water soluble packages and an applicator using open-cab, air-blast machinery. Further, HED believes exposure durations will be short-term (1 - 30 days). Intermediate-term and long-term exposures are not expected.

It is expected that some private applicators may perform all tasks, that is, mix, load and apply the material. However, HED ExpoSAC draft Standard Operating Procedure (SOP) (29 March 2000) directs that although the same individual may perform all tasks, in some cases they shall be assessed separately.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the Pesticide Handler Exposure Database (PHED) Surrogate Exposure Guide (August 1998, v 1.1). HED has adopted a methodology to present the exposure and risk estimates

separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as hand wands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-wing aircraft, groundboom tractors, air-blast sprayers, or high-pressure handwand sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical specific data were available with which to assess potential exposure to occupational pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in the PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline" that is, for workers wearing a single layer of work clothing consisting of a long sleeved shirt, long pants, shoes plus socks and no protective gloves as well as for "baseline" **and the use of protective gloves** or other PPE as might be necessary. The proposed product label involved in this assessment directs applicators and other handlers to wear the following PPE: long-sleeved shirt, long pants, shoes plus socks, chemical resistant gloves and protective eyewear.

On 12 August 1999 the HED Hazard Identification Assessment Review Committee (HIARC) met to discuss the adquacy of the toxicological database relative to myclobutanil (Memo, M. Copley, HED DOC NO 013740, "***MYCLOBUTANIL*** - Second Report of the Hazard Identification Assessment Review Committee", 2 September 1999).). RAB1 toxicologists re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment was not appropriate. A two-generation reproduction study in rats was selected. With regards to the assessment herein, the short-term duration (1 - 30 days) and the intermediate-term duration (1 - 6 months) dermal and inhalation toxicological endpoints are identified from a 2- generation reproduction toxicity study in the rat. The NOAEL is 10.0 mg ai/kg bw/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation. The HIARC identified a 50 % dermal absorption factor for use in assessing dermal exposures. Inhalation absorption is assumed to be 100 %. See Table 2.0 for a summary of exposures and risks to occupational pesticide handlers. See the ATTACHMENT for a summary of the toxicological endpoints used for risk assessment.

Table 2.0 Estimated Handler Exposure and Risk from the Use of Myclobutanil on Hops					
Unit Exposure[1] mg a.i./lb handled	**Applic. Rate[2]**	**Units Treated[3] Per Day**	**Average Daily Dose[4] mg a.i./kg bw/day**	**NOAEL[5] mg a.i./kg bw/day**	**COMBINED MOE[6]**
Mixer/Loader - Wettable Powders with Water Soluble Bags					
Dermal: No Glove 0.021 LC With Glove 0.0098 LC Inhal. 0.00024 LC	0.25 lb a.i./A	40A	Dermal: No Glove 0.0015 W Glove 0.0007 Inhal 0.00004	Dermal 10 Inhalation 10	No Glove 6,500 With Glove 13,500
Applicator - Airblast - Open Cab					
Dermal: No Glove 0.36 HC With Glove 0.24 HC Inhal 0.0045HC	0.25 lb a.i./A	40 A	Dermal: No Glove 0.0255 W Glove 0.017 Inhal 0.00075	Dermal 10 Inhalation 10	No Glove 380 With Glove 560

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.
2. Applic. Rate. = Taken from the IR4 petition for myclobutanil on hops
3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000;
4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * 0.5 (% dermal absorption) ÷ Body Weight
5. NOAEL = No Observable Adverse Effect Level; short- and intermediate term dermal and inhalation NOAEL = 10 mg a.i./kg bw/ ay.
6. Combined Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. The dermal and inhalation toxicological effects are the same, have the same NOAELs and are identified from the same study. Therefore, the dermal and inhalation exposures are summed and then divided into the NOAEL to derive MOE.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

It is possible for agricultural workers to have post-application exposure to pesticide residues during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur and which may result in post-application exposures to pesticide residues. HED has also identified Transfer Coefficients (TC) relative to the various activities which express the amount of foliar contact over time, during each of the activities identified. TC's are expressed as cm^2/hr. For hops, the highest TC is 2,000 cm^2/hr which results from harvest activities or stripping or training the vines. As a "screening" level assessment, HED herein uses the 2,000 cm^2/hr TC.

The TCs used in this assessment are from an interim TC Standard Operating Procedure (SOP) developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP # 3.1). It

is the intention of HED's ExpoSAC that this SOP will be periodically updated to incorporate additional information about agricultural practices in crops and new data on TCs. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Lacking compound specific dislodgeable foliar residue (DFR) data, HED assumes 20 % of the application rate is available as DFR on day zero after application. This is adapted from the ExpoSAC SOP No. 003 (7 May 1998 - Revised 7 August 2000).

The following convention may be used to estimate post-application exposure.

Average Daily Dose (ADD) (mg a.i./kg bw/day) = DFR $\mu g/cm^2$ * TC cm^2/hr * hr/day * 0.001 mg/μg * 1/60 kg bw

and where:

Surrogate Dislodgeable Foliar Residue (DFR) = application rate * 20% available as dislodgeable residue * $(1-0)^1$ * 4.54 x 10^8 $\mu g/lb$ * 2.47 x 10^{-8} A/cm^2.

0.25 lb a.i./A * 0.20 * $(1-0)^0$ * 4.54 x 10^8 $\mu g/lb$ * 2.47 x 10^{-8} A/cm^2 = 0.56 $\mu g/cm^2$, therefore,

0.56 $\mu g/cm^2$ * 2,000 cm^2/hr * 8 hr/day * 0.001 mg/μg * 0.5 (% dermal absorption) ÷ 70 kg bw = 0.064 mg/kg bw/day.

MOE = NOAEL ÷ ADD then 10.0 mg/kg bw/day ÷ 0.064 mg/kg bw/day = **156.**

A MOE of 100 is adequate to protect agricultural workers from post-application exposures. Since the estimated MOEs are > 100, the proposed use does not exceed HED's level of concern.

RESTRICTED ENTRY INTERVAL (REI)

Myclobutanil is classified in Acute Toxicity Category IV for acute dermal, acute inhalation and primary skin irritation. It is classified in Category I for primary eye irritation and it is a "Positive" dermal sensitizer. The Rally® label lists the REI as 24 hours.

Title 40 of the Code of Federal Regulations, § 156.208 (c) (2) states: If a product contains only one active ingredient and it is in toxicity category I by the criteria in paragraph (c) (1) of this section, the restricted-entry interval shall be 48 hours." The Federal Register Vol. 57, No. 163, 21 August 1992 page 38104 and 38142 (For 40 CFR Parts 156 and 170) indicates that "...a 48-hour REI is established for any product containing an active ingredient that is in toxicity category I (most acutely toxic category) because of dermal toxicity or skin or eye irritation."

HED suggests that the RD confirm or correct, as may be necessary, the 24 hour REI listed on the product label.

ATTACHMENT

Acute Toxicity of **Myclobutanil**

Guideline No.	**Study Type**	**MRID #(S)**	**Results**	**Toxicity Category**
81-1	Acute Oral	00141662	LD_{50} = 1.6 g/kg (M) LD_{50} = 2.29 g/kg (F)	III
81-2	Acute Dermal	00141663	LD_{50}> 5000 mg/kg	IV
81-3	Acute Inhalation	40357101	LC_{50} > 5.1 m/L	IV
81-4	Primary Eye Irritation	00141663	Severe eye irritant	I
81-5	Primary Skin Irritation	00141663	Non-irritating to skin	IV
81-6	Dermal Sensitization	40357102	Positive sensitizer	

Summary of:
The doses and toxicological endpoints for use in risk assessment

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary females 13-50 years of age	NOAEL=60 UF = 100	LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.	Developmental Toxicity - rabbit
	Acute RfD = 0.60		
Acute Dietary general population including infants and children	none		
	Acute RfD = none		
Chronic Dietary	NOAEL =2.49 mg/kg/day UF = 100	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
	Chronic RfD = 0.025 mg/kg/day		
Short-Term (Dermal)	oral NOAEL=10 mg/kg/day[1]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease	2 Generation Reproduction Toxicity - rat

		in pup weight gain during lactation.	
Intermediate-Term (Dermal)	oral NOAEL=10 mg/kg/day[1]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Long-Term (Dermal)	oral NOAEL =2.49 mg/kg/day[1]	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
Short Term (Inhalation)	oral NOAEL=10 mg/kg/day[2]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Intermediate Term (Inhalation)	oral NOAEL=10 mg/kg/day[2]	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Long Term (Inhalation)	oral NOAEL =2.49 mg/kg/day[2]	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat

[1] Use the appropriate dermal absorption factor (50%) since the NOAEL is from an oral study.
[2] Use the appropriate absorption factor (100%) since the NOAEL is from an oral study.

NOTE: ATTACHMENT taken from: Memo, M. Copley, "***MYCLOBUTANIL:*** - Second Report of the Hazard Identification Assessment Review Committee", HED DOC NO 013740, 2 SEPT 1999 and amended by the RAB1 toxicology team.

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